REMARKS/ARGUMENTS

Claims 1 – 8, 13 and 21 – 26 are pending in the instant application. **Claims 1 – 7** stand objected to under 35 U.S.C § 103(a) as being unpatentable over Ardenkjaer-Larsen et al. (US Patent No. 6,278,893) in view of Werne (US Patent No. 5,782,764). **Claim 8** stands objected to under 35 U.S.C § 103(a) as being unpatentable over Ardenkjaer-Larsen et al. (US Patent No. 6,278,893) in view of Werne (US Patent No. 5,782,764) and Kucharczyk (US Patent No. 6,026,316). **Claim 13** stands objected to under 35 U.S.C § 103(a) as being unpatentable over Ardenkjaer-Larsen et al. (US Patent No. 6,278,893) in view of Werne (US Patent No. 5,782,764) and Goldenberg (US Patent No. 5,776,093). Claims 1 – 8, 13 and 21 – 26 are pending in the instant application. The application has been amended. The claims have been amended. Claims 1, 5, 8 and 13 have been amended, claims 21 – 26 have been newly added. **Claims 9 – 12** and **14 – 20** have been cancelled. Applicant respectfully submits that none of the amendments constitute new matter in contravention of 35 U.S.C. §132. Reconsideration is respectfully requested.

Basis for Amendments

Claim 1 is based on previously presented claim 1 and has been limited to a method of therapy. The term "placed in the region in need of treatment" which has been incorporated into the claim can be found on page 3, paragraph [0029] of the published US application (US2006/0173283). The embodiment wherein a therapeutically active compound is provided via the invasive device is disclosed on page 3, paragraph [0028] and implicitly [0029] – an [invasive] device is placed in the region in need of treatment and a therapeutically active compound is instilled at the site. The embodiment wherein an MR medium is provided via

the invasive device is disclosed on page 3, paragraphs [0028] and [0029]. The embodiment wherein an MR medium is provided within the invasive device is disclosed in claim 5 and on page 4, paragraph [0046]. The term "hyperpolarized solid" has been deleted from claim 1 and thus the MR medium has been limited to a solution. The term "hyperpolarized solution of a high T1 agent" has been corrected for clarity reasons to a "solution of a hyperpolarised high T1 agent". It is apparent from the specification page 2, paragraph [0009] and [0016] in connection with [0021] and a chosen high T1 agent is hyperpolarized which will result in a "hyperpolarized high T1 agent".

Claim 5 has been amended by substituting the term "contrast medium" by the term "MR medium" for clarity reasons. Basis can be found in claim 1. The previously preferred embodiment of a cavity which is fitted with an outside duct has been made a mandatory feature of the claim.

Claim 8 has been amended by clarifying that the high T1 agent and the therapeutically active compound are identical rather than the contrast medium (which the high T1 agent is the "MR active ingredient" but which may contain other ingredient, for example a solvent) and the therapeutically active compound. Basis can be found in the specification on page 3, paragraph [0029] where it is disclosed that ".....a [therapeutically active] compound enriched with polarizable nuclei" is used. It is apparent that such a compound is the high T1 agent having polarizable nuclei (see also [0029], 4th sentence).

Claim 13 has been amended by adapting its wording to independent claim 1.

Newly added **claim 21** is based on the specification page 3, paragraph [0029], 3rd sentence.

Newly added **claim 22** is based on the specification page 3, paragraph [0027], 2nd sentence.

Newly added **claim 23** is based on originally filed claim 2.

Newly added **claim 24** is based on the specification page 3, paragraph [0028], 2nd sentence.

Newly added **claim 25** is based on the specification page 3, paragraph [0028], 3rd sentence and page 2, paragraph [0019].

Newly added **claim 26** is based on the specification page 3, paragraph [0028], last sentence and page 2, [0019], 1st sentence.

Section 103(a) Rejection

Claims 1 – 7 stand objected to under 35 U.S.C § 103(a) as being unpatentable over Ardenkjaer-Larsen et al. (US Patent No. 6,278,893) in view of Werne (US Patent No. 5,782,764). **Claim 8** stands objected to under 35 U.S.C § 103(a) as being unpatentable over Ardenkjaer-Larsen et al. (US Patent No. 6,278,893) in view of Werne (US Patent No.

5,782,764) and Kucharczyk (US Patent No. 6,026,316). **Claim 13** stands objected to under 35 U.S.C § 103(a) as being unpatentable over Ardenkjaer-Larsen et al. (US Patent No. 6,278,893) in view of Werne (US Patent No. 5,782,764) and Goldenberg (US Patent No. 5,776,093). These rejections are respectfully traversed.

Ardenkjaer-Larsen et al. disclose a method of MR investigation of a sample, preferably of a human or non-human animal body, which involves administering an MR medium comprising a hyperpolarized high T1 agent that comprises nuclei selected from the group consisting of ^{1}H, ^{3}Li, ^{13}C, ^{15}N, ^{19}F, and ^{31}P. It is further disclosed that the high T1 agent has a T1 value of at least 5 seconds at a field strength of 0.001-5 T and a temperature of 20-40 °C.

As the Examiner correctly points out, Ardenkjaer-Larsen et al. do not disclose a method of therapy wherein an invasive device is inserted into a human or non human animal body and placed in the region of treatment, and wherein an MR image of at least a part of said body containing said device is generated to visualise said device, comprising the step of providing via the invasive device a therapeutically active compound and via or within the invasive device an MR medium.

Werne discloses and invention that comprises an invasive device wherein an operative or other portion of the instrument is marked with a MR contrast agent that is appropriate to MR imaging. Werne's method includes displaying an MR image including the invasive device.

However, all embodiments disclosed by Werne have the common feature of the contrast agent being a permanent part of the invasive device, e.g. a marker stylet that contains a contrast agent encapsulated in a chamber on/in the device.

Applicant respectfully submits that such an embodiment is technically not possible if the contrast agent is a hyperpolarized high T1 agent. Such agents are produced by forcefully disturbing the thermal equilibrium spin distribution of nuclei in a chemical compound. At thermal equilibrium, the spins are equally distributed on the different spin levels and the resulting magnetization is zero. However, by disturbing this equilibrium (by e.g. applying very low temperatures and a high magnetic field) it is possible to obtain non-equal spin distribution and thus a magnetization which can directly be detected in MR imaging or spectroscopy. Said magnetization is however a temporary limited phenomenon since the spin system relaxes over time to the equilibrium with zero magnetization, when no longer subjected to the harsh conditions which forces it out of the equilibrium. Said relaxation is a relatively fast process at room temperature and "normal" magnetic field, i.e. the earth' magnetic field and thus hyperpolarized high T1 agents are usually only useful MR contrast agent over a maximum time period of 60 – 100 s (see specification of the present application, page 2, paragraph [0020]. This means that the high T1 agent needs to be hyperpolarized at the place where it is going to be used in an MR method and after hyperpolarization, it needs to be used immediately. In view of this it is apparent that an embodiment, wherein the hyperpolarized high T1 agent is a permanent part of the invasive device, e.g. being

encapsulated in a chamber on/in said device, is technically not feasible. This is mirrored by the wording of claim 1 and claim 5.

Applicant respectfully submits that **Goldenberg** (US Patent No. 5,776,093) must be applied in this context since Goldenberg discloses methods therapy by ablation. As the Examiner correctly points out, Goldenberg discloses an immunological method of ablation by administering to a subject a composition comprising and antibody or fragment thereof which is specific to a receptor on a cell or tissue targeted for ablation. However, Applicant submits that the method of Goldenberg does not include the use of an invasive device, the compositions are administered by parenteral injection (for instance col. 2, line 51 and 64). Further Goldenberg does not disclose that an MR medium (MR image enhancing agent) and a therapeutically active compound in ablation are administered together (present claim 1) or that the MR image enhancing agent is a compound effective in ablation (present claim 13). Goldenberg discloses either the administration of a an MR image enhancing agent comprising an antibody or a fragment thereof or the administration of a composition comprising and antibody or fragment thereof which is specific to a receptor on a cell or tissue targeted for ablation. Goldenberg therefore teaches away from the claims of the present invention.

Similarly, Kucharczyk et al. (US Patent No. 6,026,316) disclose a method wherein a drug delivery device is positioned at a site in the body of a patient and its position is observed by MR imaging. The drug delivery device is used to instill a drug at a region of interest.

The drug delivery device of Kucharczyk et al. is MR visible due to being an MR observable device or due to being used in the presence of MR observable compounds, e.g. an MR medium (col. 6, last paragraph). The former embodiment requires MR-visible markers on the device or RF microcoils. Both embodiments are outside the scope of the present invention. The latter embodiment may either be the drug itself, i.e. the drug is an MR medium. However, in contrary to present claim 8, in the method of Kucharczyk et al. the drug is tracked by frequency shifts caused by the drugs or agents which are added to the drug. No frequency changes need to be observed when the therapeutically active compound (drug) is a hyperpolarized high T1 agent since the MR signal from said agent is directly detected (see WO99/35508 which was included by reference to the specification, page 2, paragraph [0016]).

Hence neither Ardenkjaer-Larsen et al in view of Werne or in view of Goldenberg or in view of Kucharczyk et al. or in view of the combined disclosures of Werne, Goldenberg and Kucharczyk et al. renders the invention of **claim 1** obvious. Reconsideration and withdrawal of the rejection is respectfully requested.

Likewise, as **claims 2 – 8, 13** and **21 – 26** are directly or indirectly dependent on independent claim 1, it is Applicant's belief that these claims are patentably distinct from the prior art. Reconsideration and withdrawal of the rejection of these claims are respectfully requested.

In view of the amendments and remarks hereinabove, Applicant respectfully submits that the instant application, including claims 1-8, 13, and 21-26, is allowable over the prior art. Favorable action thereon is respectfully requested.

Any questions with respect to the foregoing may be directed to Applicant's undersigned counsel at the telephone number below.

Respectfully submitted,

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